```
? b 411
       02may06 06:46:35 User208650 Session D824.2
            $0.00    0.102 DialUnits File410
     $0.00  Estimated cost File410
     $0.00  Estimated cost this search
     $0.41  Estimated total session cost   0.220 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
   (c) 2006 Dialog

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
? sf medicine
>>>         135 is unauthorized
>>>         138 is unauthorized
>>>         162 is unauthorized
>>>3 of the specified files are not available
   You have 23 files in your file list.
   (To see banners, use SHOW FILES command)
? s rhinitis and ?loratadin?

Your SELECT statement is:
   s rhinitis and ?loratadin?

          Items   File
          -----   ----

   No files have one or more items; file list includes 23 files.
   One or more terms were invalid in 22 files.

? s rhinitis and loratadin?

Your SELECT statement is:
   s rhinitis and loratadin?

          Items   File
          -----   ----
            250     5: Biosis Previews(R)_1969-2006/Apr W4
            482    34: SciSearch(R) Cited Ref Sci_1990-2006/Apr W4
              2    65: Inside Conferences_1993-2006/Apr 28
             75    71: ELSEVIER BIOBASE_1994-2006/Apr W5
            926    73: EMBASE_1974-2006/May 02
              1    91: MANTIS(TM)_1880-2006/Feb
             12    94: JICST-EPlus_1985-2006/Feb W1
             13    98: General Sci Abs_1984-2004/Dec
            154   144: Pascal_1973-2006/Apr W2
            133   149: TGG Health&Wellness DB(SM)_1976-2006/Apr W3
            341   155: MEDLINE(R)_1951-2006/May 03
            111   156: ToxFile_1965-2006/Apr W3
              6   159: Cancerlit_1975-2002/Oct
              1   164: Allied & Complementary Medicine_1984-2006/Apr
              1   172: EMBASE Alert_2006/May 02
             69   399: CA SEARCH(R)_1967-2006/UD=14418
             24   434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
              8   444: New England Journal of Med._1985-2006/Apr W3

   18 files have one or more items; file list includes 23 files.

? rf
Your last SELECT statement was:
   S RHINITIS AND LORATADIN?
```

```
Ref        Items   File
---        -----   ----
N1           926    73: EMBASE_1974-2006/May 02
N2           482    34: SciSearch(R) Cited Ref Sci_1990-2006/Apr W4
N3           341   155: MEDLINE(R)_1951-2006/May 03
N4           250     5: Biosis Previews(R)_1969-2006/Apr W4
N5           154   144: Pascal_1973-2006/Apr W2
N6           133   149: TGG Health&Wellness DB(SM)_1976-2006/Apr W3
N7           111   156: ToxFile_1965-2006/Apr W3
N8            75    71: ELSEVIER BIOBASE_1994-2006/Apr W5
N9            69   399: CA SEARCH(R)_1967-2006/UD=14418
N10           24   434: SciSearch(R) Cited Ref Sci_1974-1989/Dec
   18 files have one or more items; file list includes 23 files.

        - Enter P or PAGE for more -
? b n1-n10
       02may06 06:49:09 User208650 Session D824.3
            $3.17    1.197 DialUnits File411
     $3.17  Estimated cost File411
     $0.80  TELNET
     $3.97  Estimated cost this search
     $4.38  Estimated total session cost   1.416 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File  73:EMBASE 1974-2006/May 02
        (c) 2006 Elsevier Science B.V.
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W4
        (c) 2006 Inst for Sci Info
  File 155:MEDLINE(R) 1951-2006/May 03
        (c) format only 2006 Dialog
  File   5:Biosis Previews(R) 1969-2006/Apr W4
        (c) 2006 BIOSIS
  File 144:Pascal 1973-2006/Apr W2
        (c) 2006 INIST/CNRS
  File 149:TGG Health&Wellness DB(SM) 1976-2006/Apr W3
        (c) 2006 The Gale Group
  File 156:ToxFile 1965-2006/Apr W3
        (c) format only 2006 Dialog
*File 156: ToxFile has resumed updating with UD20051205.
  File  71:ELSEVIER BIOBASE 1994-2006/Apr W5
        (c) 2006  Elsevier Science B.V.
  File 399:CA SEARCH(R) 1967-2006/UD=14418
        (c) 2006 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
        (c) 1998 Inst for Sci Info

      Set  Items  Description
      ---  -----  -----------
? s rhinitis and loratadin?
           89917  RHINITIS
            7049  LORATADIN?
      S1    2565  RHINITIS AND LORATADIN?
?´rd
Processing - Examined 1200 records
Processing - Examined 2400 records
      S2    1570  RD  (unique items)
? s s2 and (descarb?(5n)loratadin?)
            1570  S2
            4249  DESCARB?
            7049  LORATADIN?
             178  DESCARB?(5N)LORATADIN?
      S3      10  S2 AND (DESCARB?(5N)LORATADIN?)
```

? t/5/1-10

3/5/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE


07104486 EMBASE No: 1997368522

Pharmacokinetics of **loratadine** and pseudoephedrine following single and multiple doses of once- versus twice-daily combination tablet formulations in healthy adult males

Kosoglou T.; Radwanski E.; Batra V.K.; Lint J.M.; Christopher D.; Affrime M.B.
T. Kosoglou, Clinical Pharmacology Department, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033 United States

Clinical Therapeutics ( CLIN. THER. ) (United States) 1997, 19/5 (1002-1012)
CODEN: CLTHD ISSN: 0149-2918
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 15

The pharmacokinetic profiles of single and multiple doses of **loratadine**, **descarboethoxyloratadine** (DCL) (the major active metabolite of **loratadine**), and pseudoephedrine were determined in a randomized, open-label, two-way crossover study in 24 healthy men. Subjects received a single dose (day 1) and multiple doses (days 3 to 10) of a once-daily (QD) formulation of **loratadine** 10 mg in an immediate-release coating and pseudoephedrine sulfate 240 mg in an extended-release corn (CLAR-TIN-D(R) 24 HOUR tablets), and a twice-daily (BID) formulation of **loratadine** 5 mg in an immediate-release coating and pseudoephedrine sulfate 120 mg, with 60 mg in an immediate- release coating and 60 mg in the barrier-protected core (CLARITIN-DDelta 12 HOUR tablets) in study sessions, each separated by a 10-day washout period. Both regimens were safe and well tolerated. On day 1, plasma ***loratadine*** , DCL, and pseudoephedrine concentrations were higher following the QD formulation than following the BID formulation, as expected. On day 10, **loratadine** and DCL maximum plasma concentration (C(max)) values were, on average, 87% and 35% higher, respectively, for the QD formulation than for the BID formulation; however, the values of the area under the plasma concentration-time curve from 0 to 24 hours (AUCinf 0inf -inf 2inf 4) for **loratadine** and DCL were equivalent (90% confidence interval (CI): 83% to 110% for ***loratadine*** ; 90% to 107% for DCL). On day 10, pseudoephedrine C(max) and AUCinf 0inf -inf 2inf 4 values were equivalent (90% CI for C(max): 94% to 109%; for AUC: 91% to 106%) for the two formulations, and lower pseudoephedrine concentrations were observed from 16 to 24 hours with the QD formulation. Both ***loratadine*** /pseudoephedrine formulations produced equivalent **loratadine** and DCL AUCinf 0inf -inf 2inf 4 values and equivalent pseudoephedrine C(max) and AUCinf 0inf -inf 2inf 4 values following multiple dosing. The lower pseudoephethine concentrations in the evening with the QD formulation may minimize the potential for insomnia in patients when compared with the BID formulation.

MANUFACTURER NAMES: schering plough/USA
DRUG DESCRIPTORS:
***loratadine**--adverse drug reaction--ae; ***loratadine**--clinical trial--ct; ***loratadine**--drug therapy--dt; ***loratadine** --pharmaceutics--pr; ***loratadine**--pharmacokinetics--pk; * pseudoephedrine--adverse drug reaction--ae; *pseudoephedrine--clinical trial--ct; *pseudoephedrine--drug therapy--dt; *pseudoephedrine --pharmaceutics--pr; *pseudoephedrine--pharmacokinetics--pk; *claritin d --adverse drug reaction--ae; *claritin d--clinical trial--ct; *claritin d --drug therapy--dt; *claritin d--pharmaceutics--pr; *claritin d --pharmacokinetics--pk

MEDICAL DESCRIPTORS:
*allergic **rhinitis**--drug therapy--dt
drug formulation; drug blood level; insomnia--side effect--si; drug safety; drug tolerance; headache--side effect--si; human; male; normal human; clinical trial; randomized controlled trial; crossover procedure; controlled study; adult; article
CAS REGISTRY NO.: 79794-75-5 ( ***loratadine*** ); 345-78-8, 7460-12-0, 90-82-4 (pseudoephedrine
SECTION HEADINGS:
011 Otorhinolaryngology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reaction Titles
039 Pharmacy

3/5/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE


06326040 EMBASE No: 1995348533
Antiallergic properties of **loratadine**: A review
Bousquet J.; Czarlewski W.; Danzig M.R.
Cliniques des Maladies Respiratoire, Centre Hospitalier Universitaire, Hopital Arraud de Villeneuve,34295 Montepellier-Cedex France
Advances in Therapy ( ADV. THER. ) (United States) 1995, 12/5 (283)
CODEN: ADTHE ISSN: 0741-238X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Histamine is a major mediator of the allergic reaction, and histamine Hinf 1- receptor antagonists have a long history of clinical efficacy in a variety of allergic disorders. ***Loratadine*** is one of a new generation of antihistamines that lack central nervous system depressant or anticholinergic effects and do not cause torsades de pointes-type arrhythmias. ***Loratadine*** and other second- generation antihistamines also possess additional antiallergic properties beyond those affected through histamine Hinf 1-receptors. ***Loratadine*** and its active metabolite, **descarboxyethoxyloratadine**, help to stabilize mast cells, as evidenced by their ability to inhibit the release of histamine, leukotrienes, and prostaglandins induced by both IgE-dependent and -independent stimuli in animal and human in vitro studies. ***Loratadine*** also inhibits stimulus-induced bronchospasm, airway resistance, nasal mucous production, and nasal vasopermeability in some animal models. In patients with seasonal allergy, **loratadine** markedly reduces symptoms induced by allergen exposure. Analysis of secretory fluids and tissues after challenge indicates that **loratadine** interferes with mediator release. Recruitment of inflammatory cells to the site of the allergic insult is also disturbed by **loratadine**, suggesting that the drug may inhibit upregulation of molecules involved in cell adhesion and migration and perhaps may interfere with the cytokine cascade through its ability to stabilize mast cells and limit incursion of inflammatory cells.

DRUG DESCRIPTORS:
*allergen; *antiallergic agent--clinical trial--ct; *antiallergic agent --drug dose--do; *antiallergic agent--drug therapy--dt; *antiallergic agent --pharmacology--pd; *histamine--endogenous compound--ec; *histamine h1 receptor antagonist--pharmacology--pd; *histamine h1 receptor antagonist --drug therapy--dt; *histamine h1 receptor antagonist--drug dose--do; * histamine h1 receptor antagonist--clinical trial--ct; *leukotriene --endogenous compound--ec; ***loratadine**--pharmacology--pd; * ***loratadine**--clinical trial--ct; ***loratadine**--drug therapy--dt; ***loratadine**--drug dose--do; ***loratadine**--drug comparison--cm astemizole--clinical trial--ct; astemizole--drug comparison--cm; astemizole

--drug therapy--dt; calcium--endogenous compound--ec; cell adhesion molecule--endogenous compound--ec; drug metabolite; histamine release inhibitor--pharmacology--pd; histamine release inhibitor--drug therapy--dt; histamine release inhibitor--drug dose--do; histamine release inhibitor --clinical trial--ct; immunoglobulin e--endogenous compound--ec; placebo; prostaglandin--endogenous compound--ec; terfenadine--pharmacology--pd; terfenadine--drug therapy--dt; terfenadine--drug comparison--cm; terfenadine--clinical trial--ct
MEDICAL DESCRIPTORS:
*allergic **rhinitis**--drug therapy--dt; *allergy--drug therapy--dt; * bronchospasm; *histamine release; *rhinoconjunctivitis--drug therapy--dt airway resistance; article; blood vessel permeability; clinical trial; dose response; drug mechanism; human; inflammatory cell; mediator; nonhuman; nose mucus; provocation test; skin test
CAS REGISTRY NO.: 51-45-6, 56-92-8, 93443-21-1 (histamine); 79794-75-5 ( **loratadine**); 68844-77-9 (astemizole); 7440-70-2 (calcium); 37341-29-0 (immunoglobulin e); 50679-08-8 (terfenadine)
SECTION HEADINGS:
013 Dermatology and Venereology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

3/5/3 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE


06121120 EMBASE No: 1995151857
Inhibitory activity of-**loratadine** and **descarboethoxyloratadine** on expression of ICAM-1 and HLA-DR by nasal epithelial cells
Vignola A.M.; Crampette L.; Mondain M.; Sauvere G.; Czarlewski W.; Bousquet J.; Campbell A.M.
Clinique Maladies Respiratoires, Hopital Arnaud de Villeneuve, Centre Hospitalier Universitaire,34295 Montpellier Cedex 5 France
Allergy: European Journal of Allergy and Clinical Immunology ( ALLERGY EUR. J. ALLERGY CLIN. IMMUNOL. ) (Denmark) 1995, 50/3 (200-203)
CODEN: LLRGD ISSN: 0105-4538
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Nasal epithelial cells represent the first barrier against noxious agents and allergens. In allergic ***rhinitis*** , these cells are activated and histamine may be involved in this activation. ***Loratadine*** and one of its active metabolites, descarboethoxyloratadine, were studied for their ability to reduce the activation of nasal epithelial cells by histamine. Nasal turbinates or polyps were removed during surgery from 19 subjects, and nasal epithelial cells were recovered after enzymatic digestion. The in vitro activation of epithelial cells with histamine using an optimal dose (1 muM) and an optimal time (24 h) of incubation was studied, and the effect of **loratadine** or **descarboethoxyloratadine** (10 muM) was investigated. The expression of membrane markers (intercellular adhesion molecule-1 (ICAM-1) and a human leukocyte class II antigen (HLA-DR) was assessed by immunocytochemical analysis using an alkaline-antialkaline phosphatase (APAAP) system. The spontaneous expression of both markers was not significantly different in cells recovered from nasal turbinates or polyps, and there was a highly significant increase in the numbers of cells expressing ICAM-1 and HLA-DR following incubation with histamine. **Loratadine** or **descarboethoxyloratadine** significantly blocked these effects. This study shows a new possible antiallergic effect of Hinf 1-blockers and suggests that their effects on epithelial cells may be relevant in vivo.

DRUG DESCRIPTORS:
*HLA DR antigen--endogenous compound--ec; *antiallergic agent; *histamine --endogenous compound--ec; *histamine--pharmacology--pd; *intercellular adhesion molecule 1--endogenous compound--ec; ***loratadine** --pharmacology--pd; ***loratadine**--clinical trial--ct
histamine h1 receptor antagonist; unclassified drug
MEDICAL DESCRIPTORS:
*nose mucosa
adult; article; biopsy; clinical article; clinical trial; human; human cell ; human tissue; priority journal
DRUG TERMS (UNCONTROLLED): descarboethoxyloratadine--pharmacology--pd; descarboethoxyloratadine--clinical trial--ct
CAS REGISTRY NO.: 51-45-6, 56-92-8, 93443-21-1 (histamine); 126547-89-5 ( intercellular adhesion molecule 1); 79794-75-5 (**loratadine**)
SECTION HEADINGS:
011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

3/5/4 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE


03969544 EMBASE No: 1989138540
**Loratadine**: A nonsedating antihistamine with once-daily dosing
Barenholtz H.A.; McLeod D.C.
Department of Pharmacy, University of Michigan, Ann Arbor, MI United States
DICP, Annals of Pharmacotherapy ( DICP ANN. PHARMACOTHER. ) (United States) 1989, 23/6 (445-450)
CODEN: DAPHE ISSN: 1042-9611
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: FRENCH; ENGLISH

**Loratadine** is an addition to the class of nonsedating antihistamines which includes terfenadine, astemizole, and acrivastine. ***Loratadine*** is chemically related to the tricyclic antidepressants. Animal data have shown that insignificant amounts of **loratadine** enter the brain, and it has a threefold greater affinity for peripheral as compared with central histamineinf 1-receptors. ***Loratadine*** has one main metabolite, **descarbethoxyloratadine**, which is four times more active than the parent drug. ***Loratadine*** reaches peak plasma concentration in 1-2 hours; the metabolite does so in 3-4 hours. Their respective elimination half-lives are about 10 and 20 hours. Onset of action is within 1 hour and duration is at least 24 hours. Once-daily dosing is recommended. Generally ***loratadine*** is as efficacious as existing antihistamines in relieving symptoms of allergic **rhinitis**, urticaria, and in suppressing wheal formation. Reports of sedation and other adverse reactions are no more frequent than found with placebo. Tachyphylaxis has not been noted in humans, and there is minimal potential for drug interactions based on animal data. ***Loratadine*** and terfenadine have comparable therapeutic applications. Both have shown minimal adverse effects, but **loratadine** has a quicker onset and longer duration of action. These two agents are useful for acute allergic reactions. In contrast, astemizole has an onset of action of several days and is most useful for prophylactic treatment of seasonal allergies.

BRAND NAME/MANUFACTURER NAME: sch 434/schering
MANUFACTURER NAMES: burroughs wellcome; janssen; merrell dow pharmaceuticals; schering
DRUG DESCRIPTORS:

*histamine receptor; ***loratadine***--adverse drug reaction--ae; *
**loratadine**--pharmacology--pd; ***loratadine***--drug therapy--dt; *
**loratadine**--clinical trial--ct
acrivastine; astemizole; pseudoephedrine; claritin d; terfenadine
MEDICAL DESCRIPTORS:
*allergic **rhinitis**--drug therapy--dt; *chronic urticaria--drug
therapy--dt; *pharmacokinetics
drug absorption; drug distribution; drug elimination; drug metabolism;
sedation; short survey; human; priority journal
CAS REGISTRY NO.: 79794-75-5 ( ***loratadine*** ); 87848-99-5 (acrivastine);
68844-77-9 (astemizole); 345-78-8, 7460-12-0, 90-82-4 (pseudoephedrine)
; 50679-08-8 (terfenadine
SECTION HEADINGS:
011 Otorhinolaryngology
013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reaction Titles

3/5/5 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


13382859 Genuine Article#: 876YW Number of References: 27
Title: Inhibition of nasal polyp mast cell and eosinophil activation by
desloratadine
Author(s): Kowalski ML (REPRINT) ; Lewandowska A; Wozniak J; Makowska J;
Jankowski A; DuBuske L
Corporate Source: Med Univ Lodz,Dept Clin Immunol & Allergy, Fac Med,251
Pomorska Str/PL-92213 Lodz//Poland/ (REPRINT); Med Univ Lodz,Dept Clin
Immunol & Allergy, Fac Med,PL-92213 Lodz//Poland/; Med Univ Lodz,ENT
Dept,Lodz//Poland/; Immunol Res Inst New England,Fitchburg//MA/
Journal: ALLERGY, 2005, V60, N1 (JAN), P80-85
ISSN: 0105-4538 Publication date: 20050100
Publisher: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016
COPENHAGEN, DENMARK
Language: English Document Type: ARTICLE
Geographic Location: Poland; USA
Journal Subject Category: ALLERGY; IMMUNOLOGY
Abstract: Nasal polyp tissue which contains mast cells and eosinophils is
similar to the inflamed airway mucosa in cellular composition and
mediator content. This investigation assessed the effect of
desloratadine (DL), on activation of cells in nasal polyp tissue.
Polyps were obtained from 22 patients with chronic rhinosinusitis [nine
aspirin acetylosalitic acid (ASA)-sensitive and 13 ASA-tolerant]. Polyp
tissue was dispersed by digestion, and preincubated with DL and
incubated with anti-immunoglobulin E (IgE) or calcium ionophore. LTC4,
eosinophil cationic protein (ECP) and tryptase concentrations in
supernatants were measured by immunoassays. Desloratadine (1, 10 and 50
muM) inhibited calcium ionophore-induced LTC4 release by a mean of 29%,
50% and 63% respectively, and anti-IgE-induced LTC4 release by a mean
of 27%, 35% and 39% respectively. Calcium ionophore-induced tryptase
release was inhibited 60% and 69% by 10 and 50 muM of DL, respectively,
and anti-IgE-induced tryptase release was inhibited 33%, 47% and 66%
for 1, 10 and 50 muM of DL. Desloratadine 10 muM and 50 muM inhibited
ECP release by and 45% and 48% respectively. Polyp tissue from
ASA-sensitive patients when compared with ASA-tolerant patients
released at baseline significantly more ECP (medians 120.0 mug/ml,
range: 69.0-182.0 vs 63.4 mug/ml, range: 3.7-172.0; $P < 0.05$), but
similar amounts of tryptase and LTC4. This study demonstrated that DL
inhibits activation of both eosinophils and mast cells derived from a
site of airway mucosal inflammation.

Descriptors--Author Keywords: antihistamine ; aspirin sensitivity ; desloratadine ; eosinophils ; mast cells ; nasal polyps
Identifiers--KeyWord Plus(R): LEUKOTRIENE RECEPTOR ANTAGONIST; SEASONAL ALLERGIC **RHINITIS**; CYTOKINE RELEASE; EPITHELIAL-CELLS; HISTAMINE-RELEASE; MEDIATOR RELEASE; HUMAN BASOPHILS; IN-VITRO; **LORATADINE; DESCARBOXYETHOXYLORATADINE**
Cited References:

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BARODY FM, 2000, V55, P17, ALLERGY S64
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MASTALERZ L, 2002, V32, P949, EUR J CLIN INVEST
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SIMONS FER, 2002, V110, P777, J ALLERGY CLIN IMMUN
STOOP AE, 1993, V91, P616, J ALLERGY CLIN IMMUN
SZCZEKLIK A, 1999, V104, P5, J ALLERGY CLIN IMMUN
VIGNOLA AM, 1995, V50, P200, ALLERGY


3/5/6 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci


05347890 Genuine Article#: VR622 Number of References: 51
Title: INFLUENCE OF FOOD ON THE ORAL BIOAVAILABILITY OF **LORATADINE** AND PSEUDOEPHEDRINE FROM EXTENDED-RELEASE TABLETS IN HEALTHY-VOLUNTEERS

Author(s): NOMEIR AA; MOJAVERIAN P; KOSOGLOU T; AFFRIME MB; NEZAMIS J; RADWANSKI E; LIN CC; CAYEN MN
Corporate Source: SCHERING PLOUGH CORP,RES INST,DEPT DRUG METAB &PHARMACOKINET,MAIL STOP 2880/KENILWORTH//NJ/07033; SCHERING PLOUGH CORP,RES INST,DEPT CLIN PHARMACOL/KENILWORTH//NJ/07033; SCHERING PLOUGH CORP,RES INST,DEPT BIOSTAT/KENILWORTH//NJ/07033


Journal: JOURNAL OF CLINICAL PHARMACOLOGY, 1996, V36, N10 (OCT), P923-930
ISSN: 0091-2700
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: PHARMACOLOGY & PHARMACY


Abstract: The effect of a high-fat breakfast on the bioavailability of the components of an extended-release tablet containing 10 mg **loratadine** in the immediate-release coating and 240 mg pseudoephedrine sulfate in the extended-release core was studied in 24 healthy male volunteers in a single-dose, two-way crossover study. The drug was administered after a 10-hour overnight fast or within 5 minutes of consuming a standardized high-fat breakfast. Serial blood samples were collected over a 48-hour period, and plasma was analyzed

for **loratadine** and its active metabolite ***descarboethoxyloratadine*** (DCL), and pseudoephedrine. For pseudoephedrine, maximum concentration (C-max) and area under the concentration-time curve extrapolated to infinity (AUC0-(infinity)) were similar after both treatments, indicating no relevant food effect on the bioavailability of pseudoephedrine. Also, the absorption profiles of pseudoephedrine (from Wagner-Nelson analysis) were sim ii ar for the fed and fasted treatments, indicating no apparent differences in absorption. Plasma concentration-time profiles and values for C-max and AUC0-(infinity) of DCL were similar for the two treatments, indicating no relevant food effect on the pharmacokinetics of DCL. In contrast, for ***loratadine*** , administration with food resulted in a significantly increased mean C-max (53%) and AUC from time zero to the final quantifiable sample (AUCtf) (76%), However, the resultant C-max and AUC of **loratadine** under fed conditions were well below those previously obtained at steady-state after multiple-dose administration of **loratadine** (40 mg/day) that were shown to be safe and well-tolerated in several clinical studies. The effect of food on the bioavailability and pharmacokinetic profiles of the components of a combination **loratadine**/pseudoephedrine extended-release tablet is not likely to be clinically significant.

Identifiers--KeyWords Plus: SEASONAL ALLERGIC **RHINITIS**; NON-SEDATING ANTIHISTAMINE; SENSITIVE ASSAY; HUMAN PLASMA; EFFICACY; SAFETY; PHARMACOKINETICS; TRIPROLIDINE; COMBINATION; TERFENADINE

Research Fronts: 94-0954 001 (NONSTEROIDAL ANTIINFLAMMATORY DRUGS; ISOZYME-SELECTIVE PHOSPHODIESTERASE INHIBITORS; TREATMENT OF ACID-RELATED DISEASE)

94-1191 001 (TERFENADINE METABOLISM; SELECTIVE SEROTONIN REUPTAKE INHIBITOR; DEPRESSION MANAGEMENT; PHARMACODYNAMICS OF PAROXETINE; H-1-RECEPTOR ANTAGONISTS)

94-1981 001 (ABSOLUTE BIOAVAILABILITY; DRUG DISSOLUTION; IN-VITRO IN-VIVO CORRELATIONS; ONE-COMPARTMENT BODY MODEL; SOLID DISPERSIONS; FIRST-ORDER ELIMINATION)

94-5128 001 (INTRAMUSCULAR DICLOFENAC SODIUM FOR POSTOPERATIVE ANALGESIA; LAPAROSCOPIC STERILIZATION; REDUCTION OF PAIN)

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3/5/7 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)


12099752 PMID: 15992014
Therapeutic advantages of third generation antihistamines.
Handley D A; Magnetti A; Higgins A J
Sepracor, Inc., 111 Locke Drive, Marlborough, MA 01752, USA.
Expert opinion on investigational drugs (England) Jul 1998, 7 (7) p1045-54, ISSN 1744-7658--Electronic Journal Code: 9434197
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Document type: Journal Article
Languages: ENGLISH
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A third generation of antihistamines is emerging for the treatment of allergic ***rhinitis*** and chronic urticaria. First generation antihistamines are among the most widely used drugs in the world, and provide symptomatic relief from allergies and the common cold to millions of patients, mainly in OTC combination preparations. Their full potential is limited by the sedation caused by their effects on histamine receptors in the brain. Second generation antihistamines (terfenadine, astemizole, **loratadine** and cetirizine), which block peripheral H1 receptors without penetrating the blood-brain barrier, were developed and introduced from 1981 onwards to provide comparable therapeutic benefit without the CNS side-effects. Although largely successful in this goal, terfenadine and astemizole were found to cause potentially serious arrhythmias when plasma concentrations became elevated subsequent to impaired metabolism. It was established that the cardiac toxicity was mainly due to the parent drugs. As active metabolites could account for most of the clinical benefit, the goal for the third generation of antihistamines became to develop therapeutically active metabolites that were devoid of cardiac toxicity. The first of these drugs, fexofenadine (the active metabolite of terfenadine), was approved in July 1996, after an unusually rapid development programme. Its introduction set a new standard of safety that led the FDA to request the withdrawal of terfenadine in 1997 on the grounds that a safer version of an equivalent drug was now available. Norastemizole and **descarboethoxy loratadine** , the metabolites of astemizole

and ***loratadine*** , respectively, are also in clinical development. These offer comparable or superior clinical benefits.
Record Date Created: 20050704
Record Date Completed: 20050721

3/5/8 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


133266736 CA: 133(19)266736c PATENT
Preparation of fluorinated descarboethoxyloratadine for treatment of allergic and related disorders.
INVENTOR(AUTHOR): Piwinski, John J.; Schumacher, Doris P.; Aronov, Evgeny ; Khusid, Anatoliy
LOCATION: USA
ASSIGNEE: Schering Corporation
PATENT: PCT International ; WO 200057880 A1 DATE: 20001005
APPLICATION: WO 2000US8080 (20000327) *US 281115 (19990329)
PAGES: 19 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-031/445A; A61P-011/02B; A61P-011/06B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CR; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; HR; HU; ID; IL; IN; IS; JP; KG; KR; KZ; LC; LK; LR; LT; LU; LV; MA; MD; MG; MK; MN; MX; NO; NZ; PL; PT; RO; RU; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; US; UZ; VN; YU; ZA; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS ; MW; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA227016 Heterocyclic Compounds (One Hetero Atom)
CA201XXX Pharmacology
IDENTIFIERS: fluorodescarboethoxyloratadine prepn allergy inhibitor, loratadine fluoro descarboethoxy prepn allergic rhinitis treatment, antihistamine fluorodescarboethoxyloratadine prepn
DESCRIPTORS:
Nose...
allergic rhinitis, treatment; prepn. of fluorinated descarboethoxyloratadine for treatment of allergic and related disorders
Allergy inhibitors... Antihistamines...
prepn. of fluorinated descarboethoxyloratadine for treatment of allergic and related disorders
CAS REGISTRY NUMBERS:
125743-80-8 298220-99-2P prepn. of fluorinated descarboethoxyloratadine for treatment of allergic and related disorders

3/5/9 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


129180143 CA: 129(14)180143n PATENT
Lactose-free, non-hygroscopic and anhydrous pharmaceutical compositions of descarboethoxyloratadine
INVENTOR(AUTHOR): Redmon, Martin P.; Butler, Hal T.; Wald, Stephen A.; Rubin, Paul D.
LOCATION: USA
ASSIGNEE: Sepracor, Inc.
PATENT: PCT International ; WO 9834614 A1 DATE: 19980813
APPLICATION: WO 98US2328 (19980206) *US 37325 (19970207) *US 45184 (19970430) *US 53050 (19970721)
PAGES: 34 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:
CLASS: A61K-031/445A
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; GW; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA263006 Pharmaceuticals
IDENTIFIERS: lactose free nonhygroscopic descarboethoxyloratadine, descarboethoxy loratadine pharmaceutical
DESCRIPTORS:
Blood vessel...
disorders; lactose-free, non-hygroscopic and anhyd. pharmaceutical compns. of descarboethoxyloratadine
Allergic rhinitis... Analgesics... Capsules(drug delivery systems)...
Coatings... Decongestants... Dermatitis... Diabetic retinopathy...
Tablets(drug delivery systems)...
lactose-free, non-hygroscopic and anhyd. pharmaceutical compns. of descarboethoxyloratadine
CAS REGISTRY NUMBERS:
51-45-6 biological studies, -induced disorders; lactose-free, non-hygroscopic and anhyd. pharmaceutical compns. of descarboethoxyloratadine
9004-32-4 9004-62-0 9004-64-2 9004-65-3 9004-67-5 9032-42-2
37353-59-6 film-former; lactose-free, non-hygroscopic and anhyd. pharmaceutical compns. of descarboethoxyloratadine
50-78-2 103-90-2 15687-27-1 22071-15-4 22204-53-1 100643-71-8
lactose-free, non-hygroscopic and anhyd. pharmaceutical compns. of descarboethoxyloratadine

3/5/10 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


125177434 CA: 125(14)177434v PATENT
Methods and compositions for treating allergic rhinitis and other disorders using descarboethoxyloratadine
INVENTOR(AUTHOR): Aberg, A. K. Gunnar; Mccullough, John R.; Smith, Emil R.
LOCATION: USA
ASSIGNEE: Sepracor, Inc.
PATENT: PCT International ; WO 9620708 A1 DATE: 960711
APPLICATION: WO 95US15995 (951211) *US 366651 (941230)
PAGES: 35 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-031/44A
DESIGNATED COUNTRIES: AL; AM; AU; BB; BG; BR; BY; CA; CN; CZ; EE; FI; GE; HU; IS; JP; KG; KP; KR; KZ; LK; LR; LS; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; TJ; TM; TT; UA; UZ; VN DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA263006 Pharmaceuticals
CA201XXX Pharmacology
IDENTIFIERS: allergic rhinitis treatment descarboethoxy loratadine
DESCRIPTORS:
Neoplasm...
avoidance of promotion of; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
Heart,disease, arrhythmia...

avoidance of; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
Electric activity...
cardiac rectifying potassium current; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
Receptors,histaminic H1...
descarboethoxyloratadine binding to; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
Analgesics... Antihistaminics... Antipyretics... Cottonseed oil... Eye,disease, diabetic retinopathy... Lecithins... Nose,disease, rhinitis, allergic... Olive oil... Pharmaceutical dosage forms,capsules... Pharmaceutical dosage forms,capsules, soft... Pharmaceutical dosage forms,tablets... Soybean oil...
methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
Urticaria...
treatment of; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
CAS REGISTRY NUMBERS:
7631-86-9 biological studies, colloidal; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
9035-51-2 biological studies, inhibition of, avoidance of; methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
9004-34-6 9005-25-8 biological studies, methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine
63-42-3 557-04-0 79794-75-5 100643-71-8P methods and compns. for treating allergic rhinitis and other disorders using descarboethoxyloratadine